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SCIENTIFIC INSTITUTIONS IN THE UNITED STATES CONNECTED WITH THE SEARCH FOR, AND THE STUDY OF, ANTIBIOTICS (USSR)

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G. K. Skryabin

In February 1958 the Academy of Sciences, USSR sent me on six months' detached duty to the Institute of Microbiology of Rutgers University which is located near New York, in the city of New Brunswick, New Jersey. At this time the Institute was directed by the discoverer of streptomycin, neomycin, and other antibiotics, the Nobel Prize winner, Professor Selman Waksman.

I conducted experimental work based at this Institute under the direct guidance of Professor Waksman.

Along with constant work at the Institute of Microbiology, I made trips to New York, Washington, Chicago, Boston, Philadelphia, Peoria, Urbana, and to other cities in which I visited the most important scientific centers in the field of general microbiology. This permitted me to obtain a quite complete picture of the basic trends of work in the search for and the study of antibiotic substances of microbic origin.

American colleagues provided me the opportunity to acquaint myself with the production of antibiotics in the United States. This production also determines the scale of research work in this field.

The Antibiotic Industry of the United States. Production of Antibiotics in the United States

The United States is the basic supplier of antibiotics to the majority of the countries of the world. The antibiotic industry there competes successfully with the most important producers of antibiotics--Japan, France, and Italy.

The network of antibiotics plants in the United States is very extensive. Such very large pharmaceutical firms as Pfizer, Squibb, Eli Lilly, Abbott, Merck, and many other companies are engaged in the production of antibiotics. These companies locate their plants not only in the territory of the United States, but also in many other countries of the world. The Squibb Company can serve as an example of this. This firm, in addition to having plants in the United States, has plants in France, England, Italy, Canada, Turkey, India, Brazil, Denmark, West Germany, Argentina, and Mexico.

It should be noted that the antibiotics plants of the United States are at present producing considerably less than their planned capacity would permit.

I was afforded the opportunity to become familiar with the Squibb, Merck, Abbott, Schering, and Pfizer plants, which are equipped with the most advanced technology. The majority of the plants are equipped with 70,000-liter ferments /Translator's note: Presumably fermentation tanks/ Some of them have 20,000-liter and 30,000-liter facilities. All the plants I inspected had at their disposal a large number of such tanks.

It is necessary to note the high level of automation in the antibiotic plants of the United States. Taking samples of culture liquids to determine activity and for biological studies, addition of defoaming agents, delivery of air through bubblers, pH regulation, pressure regulation in ferments--all these operations are carried out automatically. As a rule, observation of a process is centralized. The work of all fermentation tanks is indicated on the control panel of the fermentation department.

Well-adjusted automatization in the plants has markedly reduced the quantity of nonsterile fermentations, which in turn has led to increased production of antibiotics.

When visiting plants, I was impressed by well-equipped departments for chemical purification of antibiotics. All the antibiotics plants were equipped with excellent laboratories. Many plants were served by company scientific research institutes which, as a rule, were located at the same site as the main plant of the company.

The extensive network of antibiotics production facilities, the high mechanization of these plants have permitted the United States to occupy one of the leading places in the world in the production of antibiotic substances.

I shall present brief official items of information on the production of the most important antibiotics in the United States. It is necessary to bear in mind at the same time that publication of this information there is extremely limited.

In January 1958, 29,845 billion international units of penicillin, 6,984 kilograms of streptomycin, 20,872 kilograms of dihydrostreptomycin, and 17,452 kilograms of tetracycline (achromycin) were produced in the United States.

It is interesting to compile data on the production of tetracycline. Although 99,800 kilograms of tetracycline was produced in 1956, in January 1958 alone, 17,500 kilograms was obtained in the plants in the United States. Thus, the production of this most important antibiotic increased more than two times. The production of antibiotics with a wide spectrum of action, such as chlortetracycline, oxytetracycline, neomycin, and other preparations increased sharply. Along with this, in 1958 the streptomycin output increased sharply by increasing the production of dihydrostreptomycin--a more active and less toxic preparation.

It should be noted that the industry of the United States has mastered the production of a number of new antibiotics of actinomycetic origin which are of great importance to medicine. Such antibiotics include, in the first instance, the antituberculosis preparation kanamycin, the antibiotic oliandomycin, amphotericin, ristocetin, and others.

The antibiotics industry of the United States produces a large assortment of antibiotic substances for medical needs and for animal husbandry and agriculture.

At present 28 antibiotics are being produced in the United States, not counting the huge number of their different medicinal forms. I am presenting a list of these antibiotics.

1. Penicillin. 2. Streptomycin. 3. Dihydrostreptomycin. 4. Bacitracin. 5. Chlortetracycline. 6. Oxytetracycline. 7. Tetracycline. 8. Chloramphenicol. 9. Nystatin. 10. Neomycin. 11. Cycloserin. 12. Oleandomycin. 13. Novobiocin. 14. Amphomycin. 15. Ristocetin. 16. Amphotericin. 17. Polymyxin. 18. Biomycin. 19. Carbominicin. 20. Thyrotracin. 21. Fumagiliy [transliterated].

22. Erythromycin. 23. Thiostrepton. 24. Hygromycin. 25. Antidion. 26. Framycetin. 27. Vankomitsin /Transliterated/. 28. Kanamycin.

The production of neomycin, which is used in medicine in quantities not surpassed by streptomycin, is established on a very large scale.

Antibiotic substances are used to an extremely wide extent for the needs of animal husbandry. In addition to a large quantity of special preparations for veterinary purposes, antibiotics are used as additives to the fodder rations of farm animals. As a rule, all antibiotic plants in the United States use the by-products of the antibiotic industry to obtain additives for mixed feeds for animals. Dried mycelium of the producers of antibiotics is most frequently used. This mycelium finds a wide demand in the American agricultural market.

In concluding this brief analysis of the production of antibiotic preparations in the United States, it is necessary to point out that the producers of the different antibiotics used here are distinguished by very great activity.

Network of Scientific Research Institutions Connected with the Search for and Study of Antibiotic Substances

The network of scientific research institutions occupied with problems of searching out and studying antibiotic substances is extremely extensive in the United States. In the first instance, it is essential to note the large number of institutes and laboratories of the different pharmaceutical companies. Such institutes as Merck, Squibb, Pfizer, Abbott, Schering, Eli Lilly, Bristol Laboratory, and many others are scientific research combines in which work large groups of scientists who are occupied with the search for and the study of antibiotic substances. The basic work on antibiotics is done within the walls of these institutes. Along with the company institutes, this same work is also being conducted in many departments of different American universities. Some institutes of the Department of Agriculture are carrying on work to search for antibiotics for the needs of agriculture.

As we have already pointed out, the majority of the company institutes is located near the antibiotic plants which are the production bases of these institutes.

The overwhelming majority of scientific research institutes which are occupied with problems connected with the search for and the study of antibiotics have semiproduction facilities for conducting semiproduction experimental work /Translator's note: Presumably pilot plants/. The majority of these facilities are well equipped and are quite completely automatized.

While on detached duty in the United States, I visited a large number of different institutions which were conducting work on general microbiology and on antibiotics. I shall pass on to a brief analysis of the scientific research institutions of the United States which are the chief scientific centers for the search for and the study of antibiotic substances of microbe origin.

1. The Institute of Microbiology of Rutgers University

The Institute of Microbiology is located in a new building in the suburbs /sic/ of New Brunswick. The Institute was built several years ago. Up to the time of my departure, Selman Waksman was director of the Institute. In September 1958, Professor Waksman reached 70 years of age and was retired and the post of director was occupied by a former scientific work of the Squibb Company, Doctor Limpe /Transliterated/.

The scientific staff of the Institute is not large, but is highly skilled. Co-workers of the Institute discovered new antibiotics of actinomycetic origin--streptomycin, neomycin, kandidin, kandicidin, erlichin, and many others. The personnel of the Institute have a great deal of experience in searching out and studying new antibiotics.

At present the task of the Institute is to develop new methods for searching out antibiotics of actinomycetic origin. Along with these projects, the Institute is carrying out a search for the producers of new anti-tumor, antivirus, and fungicidal antibiotics.

The new fungicidal antibiotics kandidin and kandicidin, antibiotics of the polyene group, are under study in the laboratory of Doctor Le Chevalier.

In 1958 chemical purification of kandidin was carried out in the Institute. It turned out that this antibiotic was undisputably different from the antibiotics amphotericin produced by Squibb. Projects are going on in Doctor Le Chevalier's laboratory to search out strains which will produce antivirus and anti-cancer antibiotics.

A search for producers of anti-cancer antibiotics is being conducted in the laboratory of Doctor Pew, whose work is conducted in close contact with Professor Waksman. In this laboratory the basic work is done on animals and on tissue cultures.

The largest laboratory of the Institute is that of Professor Gruppe /Transliterated/. Professor Gruppe, who is a well-known American virologist, enjoys great authority among the co-workers of the Institute. Work on searching for antivirus preparations is being conducted in Professor Gruppe's laboratory. Several antivirus antibiotics, including erlichin, were discovered in this laboratory. The preparation xerosin has been

studied for a long time in this laboratory. It was found that this preparation has splendid antipyretic properties but its chemical study is exceedingly complicated. At present this preparation has been transferred to the Merck and Squibb Institutes for chemical study. It is important to note that the preparation is not at all toxic.

An enormous amount of work is being done in the laboratory to find effective methods for searching out antivirus antibiotics. Professor Gruppe considers that out of 250 cultures of Antinomyces studied, six show an inhibiting action on the model Rous sarcoma virus. The basic object of study in the laboratory is Actinomyces. The antivirus and anti-cancer activity of Actinomyces are more pronounced in the mycelium.

Doctor Shafner's laboratory, of chemistry type, does chemical work on order for all sections of the Institute. At present the people in the laboratory are studying the isolation and purification, the structure and biosynthesis of polyene antibiotics; they are studying the purification and isolation, the differentiation and structure of streptotriiny /Transliterated. May be streptothryins/; also the isolation and purification of antibiotics of the neomycin complex. It should be pointed out that a great amount of work is being done in the section on clarifying the structure of Kaponulin /Transliterated/.

In the work of Doctor Shafner's laboratory, a great deal of attention is devoted to the isolation, purification and differentiation of Staroidy /Transliterated. Apparently steroids/, obtained as a result of their microbiological transformations. The microbiological part of the work is being done by Doctor Grinshpan /Transliterated/.

A group headed by the great geneticist of microorganisms, Dr. Shibalsky, is functioning in the Institute of Microbiology in the study of the genetics and selection of producers of antibiotics. At present Doctor Shibalsky and his group are working on the selection of neomycin strains. A great deal of work is being done on the problem of obtaining biochemical mutants in Actinomyces.

The Institute has a small group of microbiological taxonomists who work on Actinomyces and are headed by Professor Waksman (the leading co-worker of this group is Doctor Gardon). He is also fulfilling the function of director of the Museum of Microorganisms.

The work on the taxonomy of Actinomyces is being done on the basis of this museum. A large quantity of producers of antibiotic substances isolated in all countries of the world have been concentrated in this museum. As a rule, a majority of producers of new antibiotics are received in this museum immediately after announcements concerning them appear in the open press. It seems to us that this museum is the most complete repository of different producers of antibiotic substances of actinomycetic origin.

The work on taxonomy amounts to study of the morphological and physiological peculiarities of the strains found in the museum collection. Professor Waksman is now working on the compilation of a four-volume monograph on actinemyces.

In addition to the laboratories connected with the problem of antibiotics, there are several groups in the Institute of Microbiology of Rutgers University whose work is not directly connected with this problem. We shall dwell on the most important orientations of these groups.

The Laboratory of Professor Heidelberger. Professor Michael Heidelberger is one of the greatest specialists in the field of immunology. He is now working with pneumococci. He has obtained a chemically pure substance from the membrane of the cell of a pneumococcus. This substance causes stable immunity in man. A dose of 50 micrograms of the antigen obtained in the laboratory protects man from the disease. This antigen is a polysaccharide of the cell membrane. It is important to note that the substance obtained solely from the membrane is not sufficient to achieve immunity in the rabbit. Antigen from the entire cell is necessary. The task facing Professor Heidelberger is to find the connection between the chemical structure and the immunological activity of this substance.

The work being conducted in the laboratory by Professor Braun, who is well known to Soviet research workers in the genetics of microorganisms, is of interest. The basic problem which is now being worked out in his laboratory is obtaining specific antibodies to DNA isolated from different sources. It is well known that DNA in vivo is quickly decomposed by enzymes and does not succeed in forming antibodies. In the laboratory of Professor Braun, phenol has been used in the work with the brucellosis bacillum. It was found that when DNA was extracted with phenol they did not obtain pure DNA, but extracted a protein complex of DNA which was very stable in respect to enzymes. This complex contained about 20 per cent protein. It was shown that when phenol was used for extraction protein complexes of DNA were formed which, when injected into animals caused the formation of antibodies. This reaction was extremely specific. The discovery permits one to assume the solution of the practically important problem of obtaining protein complexes of DNA from different tumors which can be used to aid in diagnosis and treatment of tumors.

Experiments are being conducted in Professor Braun's laboratory on obtaining antibodies against lymphosarcomas. As of very recent times, positive results have been achieved in treating animals with serum against lymphosarcoma obtained in the laboratory.

Professor Braun has found a number of chemical substances which inhibit the transition of irregular forms of microorganisms into smooth forms which are the most pathogenic. It has been discovered that when salmine is injected in vivo, it retards the formation of the smooth forms. This way it turned out that salmine possesses interesting therapeutical properties. This work is of great theoretical importance and undoubtedly can find wide practical application, for it opens a new path for chemotherapy--combat with smooth (pathogenic) forms of microorganisms.

In conclusion, we wish to discuss the work of a small group under Doctor Forel. This biochemical laboratory works in two closely connected orientations. Doctor Forel is studying the synthesis of animo acids with microorganisms and is carrying out studies on comparative enzymology. He has shown convincingly that the biosynthesis of animo acids in different groups of microorganisms is different and that it is fundamentally similar in groups that are taxonomically close. Numerous biochemical mutants, indicators of different amino acids, have been obtained in Doctor Forel's laboratory. A large part of them are specific to one amino acid. Penicillin is widely used in the laboratory to obtain mutants.

All the laboratories of the Institute of Microbiology are very well equipped with modern instruments. One is impressed particularly with the splendid chemical equipment. The Institute has a Craig apparatus for /measuring/ point distribution, improved automatic ultraviolet spectrophotometer, an infraction spectrophotometer, and other instruments of the very newest systems. The Institute of Microbiology has a large library which receives all journals on microbiology from all countries of the world.

One should point out that the scientific staff of the Institute is also partially occupied with teaching work. The Institute of Microbiology, which is included in Rutgers University, trains highly skilled microbiologists. This training, as a rule, is finished upon completing the doctoral dissertation. In addition, many foreign specialists work on probation in the Institute every year.

2. The Merck Institute

Merck is one of the largest pharmaceutical companies in the United States. It produces penicillin, streptomycin, dihydrostreptomycin, and novomicin.

We inspected the laboratory for studying and searching out antibiotics which was located in Rahway, New Jersey. The director of the Microbiological Laboratory is Doctor Budrov /Transliterated/. The basic objective of the laboratory is to find antibiotics against tumors, viruses, and bacteria.

The Institute receives strains of antagonistic microorganisms from Europe from many plant laboratories which are connected with the Merck Company by debt. Thus, the firm receives an enormous quantity of different microorganisms which are producersof antibiotics in payment for money which the plants owe the company.

The object most frequently studied by the Institute is Actinomyces. Along with this, work is being done on fungi and bacteria.

It must be noted that the Merck Laboratory studies only cultures of microorganisms which are outstanding in respect to some properties or other, the basic choice of strains goes on to the stage of culture liquid or to the stage of very weak purification. The new antibiotic novomyocin was developed in the Merck Institute and is produced under the factory name "katomycin." The Institute is making an intense search for antibiotics of a wide spectrum of action. All differentiation of antibiotics is likewise carried out in the cultural liquid stage by means of paper chromatography. Paper electrophoresis is widely used in the Institute. Cross resistance is used as a supplementary method.

Search for fungicidal antibiotics is carried out only for the needs of plant growing.

The Institute devotes a great deal of attention to searching for anti-tumor antibiotics. Of the great mass of antagonistic cultures which are received, only those cultures are selected which differ morphologically from the standard strains which are kept in the Institute. All research on inhibition of tumors is conducted at the cultural liquid stage, not with purified preparations.

A group of scientists is working actively in the Merck Institute on searching out new growth factors which are produced by microorganisms. The objectives of this laboratory is the search for new growth factors in animals.

Special attention is devoted in the Institute to a search for microorganisms which transform steroids. The Merck Company produces cortisone, hydrocortisone, prednisone, prenisolone, and fluorocortisone, and makes extensive use of microorganisms.

Research work on vitamin B_{12} is being done in the Merck Institute.

The Institute is housed in a good, spacious building located on the grounds of a company plant. It has a museum of living cultures.

3. The Squibb Institute

As pointed out previously, the Squibb Company is one of the largest antibiotics companies in the United States. Squibb produces streptomycin, dihydrostreptomycin, penicillin, oxytetracline, nystatin, neomycin B, amphotericin B, and thiostreptone. Squibb has a patent on the last two antibiotics. The Squibb Company owns about 20 plants which produce antibiotics in many countries of the world.

A large institute was established in the city of New Brunswick which serves all Squibb plants. This institute has a branch for searching for antibiotics in Buenos Aires (Argentina).

Doctor Donovik [Transliterated] is the head of the microbiological department of the Institute. The Institute has departments of biochemistry, technology, pharmacology, and organic chemistry.

All sorts of work is being done in the Institute on possible uses of microorganisms in the pharmaceutical industry--research on antibiotics, growth factors, and steroids.

As we have pointed out previously, the original isolation of producers from the soil is done in the branch of the Institute in Argentina.

The work on antibiotics includes searching out preparations against bacteria, fungi, viruses, and tumors.

Antivirus and anti-tumor preparations are being sought for in Actinomyces, fungi, and algae.

The Squibb Company now has 15 preparations which inhibit the development of tumors in animals. All these preparations are being studied in detail. Clinical tests are not being conducted as yet.

Development of processing technology in the Squibb Institute is conducted in splendidly equipped experimental facilities. According to many American specialists, the Squibb production facilities are the best in the world. All facilities are automatized. Regulation of air, temperature, defoaming, pH measurement, and pressure are automatized.

Experiments with antibiotics, steroids, and vitamin B_{12} are being conducted with the facilities. All technology is developed with these facilities.

4. The Abbott Company Laboratory

The laboratory of the Abbott Company is located in the state of Illinois, 60 miles from Chicago (the railroad station is North Chicago). The laboratory is located on the grounds of a large pharmaceutical plant of this company. It is a large scientific research institute in which more than 400 Doctors of Science are working. More than 3,000 persons are working in the plant.

The Abbott Company is one of the largest pharmaceutical companies in the United States. It produces antibiotics and some other products (aspirin, saccharin, and others).

Of the antibiotics, the company produces penicillin, erritromitsin /Transliterated, possibly erythromycin/, ristocetin (spontin), aureomycin, and nemycin. In addition, biocitracin is packed at the plant. The company produces ghiberellin acid. The antibiotic spontin was discovered in the Abbott Laboratory. This antibiotic is produced by a species of Nocardia.

Extensive searches are being conducted in the laboratory for antibiotic substances against bacteria, viruses, and tumors. Several thousand cultures of microorganisms pass through the first stage of study every month. Actinomyces form the basic object of study.

It is necessary to emphasize that all primary research--toxicity, therapeutic effect, and differentiation of antibiotics--is conducted at the culture liquid stage. Antibiotics which have proved themselves in these tests pass on for thorough study.

A great deal of work is being done in the Abbott Laboratory on studying preparations for the needs of animal husbandry. All mycelium, the producer of the antibiotics, which are the end product of production, is dried, ground, and is sold as a preparation for the needs of animal husbandry.

The Institute is well equipped and is located in a large building. The Institute has large pharmacological and chemical laboratories; the technology for obtaining the preparation Galimitsidin /Transliterated, English equivalent not known/; this preparation contains the antibiotic erythromycin and is designed for the needs of veterinary medicine.

Doctors Singlyar /Transliterated/ and Peterson head the Microbiological Department and the Physiological Department, respectively.

5. The Therapeutic Institute of the Pfizer Company

The Pfizer Company has a large research institute in the vicinity of Brooklyn in the city of New York. For reasons not under my control it turned out to be possible to inspect only the therapeutic section of this institute, which was located in the city of Maywood, New Jersey.

The Pfizer Company produces the following antibiotics: terramycin, tetracycline, oliandomycin, triocetiloleandomycin, biomycin, magnomycin. All these antibiotics were discovered in the Pfizer Institute. In addition, Pfizer produces streptomycin, dihydrostreptomycin, neomycin, the polymexin complex, bacitricin, and penicillin.

The search for antibiotics is conducted under the leadership of Doctor Sobin [Transliterated, possibly Sabin], who is the discoverer of terramycin, tetracline, and oleandomycin. The search for antibiotics at the Institute is being conducted on a very large scale.

The basic object of study is Actinomyces. All searches for anti-tumor antibiotics are conducted in the Therapeutic Institute in the city of Maywood, where we succeeded in becoming acquainted with the work of this institute.

The director of this institute is Doctor Weber. The Therapeutic Institute in Maywood has a department for testing antibiotics on tumors. The search for anti-tumor antibiotics is being conducted with cultures obtained from the institute in Brooklyn.

In contrast to the majority of the research institutes in America, pharmacological studies are conducted solely with purified preparations.

We succeeded in becoming acquainted with a laboratory which searches for antibiotics against helminths and protozoa. Doctor Lynch heads this Laboratory of Parasitology. Special attention is being devoted to searching for remedies against schistosomiasis. It was discovered in the laboratory that terramycin is a good antihelminthic.

The Institute has a well organized department of radiochemistry. Terramycin tagged with C_{14} is used in this department.

In addition to antibiotics and steroids, the Pfizer Company is developing ghiberellin, citric acid, itaconic and gluconic acids, and lysine. This is not surprising as the Pfizer Institute carries on research work in these fields.

The Pfizer Company devotes much attention to projects connected with the production of antibiotic preparations for the needs of animal husbandry and plant culture. The Pfizer Company has organized a department of the Institute in the state of Indiana which is connected with study of the problems of antibiotics in agriculture.

6. The Schering Institute

The large Schering Scientific Research Institute and Schering Plant are located in the city of Bloomfield, New Jersey.

The Schering Company is one of the largest companies which produces chemicals and pharmaceuticals. At present Schering is working on antibiotics.

The most interesting feature in the work of the Schering Institute is their research program on steroids. All the Schering Company steroids are obtained by microbiological means.

The Institute developed methods for obtaining cortisone, hydrocortisone, prednisone, and prednisolone.

Prednisone and prednisolone are steroids obtained with the aid of microorganisms from cortisone and hydrocortisone. The microbiological method for obtaining prednisone and prednisolone was discovered in the in the Schering Company Institute.

A search for microorganisms which transform steroids is being carried out in the Schering Institute. Actinomyces, fungi, and bacteria are the objects of study.

It was shown by the work in the Schering Institute that the amount of air entering the fermentation tank has an enormous influence in the microbiological transformation of steroids. It was established by experiment that it was best of all to use molecular oxygen for these purposes. The pH number and the culturing temperature which are very important in the production of antibiotics do not play a large role in the production of steroids.

Doctor Chernyy [Transliterated], who recently visited the Soviet Union, is the head of the research on microbiological transformations of steroids. Doctor Waterman, who is at the same time vice president of the company on research work, heads the institute.

The work of the Schering Institute on steroids is closely linked with the work on microbiological transformation of steroids being conducted by the Institute of Microbiology of Rutgers University.

The Schering Company intends to begin extensive production of antibiotics, for which purpose it is now conducting a great amount of work on searching out new antibiotics.

7. The Laboratory of David Gottlieb in Illinois University

The laboratory of Professor Gottlieb is the Department of Phytopathology in the State University in the city of Urbana.

Actually, the entire staff of the laboratory is working on the search for and the study of antibiotics and their producers.

The laboratory is small, but well equipped. The objectives of the laboratory can be divided into several problems.

A. The search for fungicidal antibiotics. The laboratory does not conduct any search for antibacterial preparations, for the laboratory cannot compete with the huge industrial institutes. It concentrates attention only on fungicidal antibiotics. Here are several new polyene antibiotics which are now passing through the study stage. The task of the laboratory is to search for fungicidal antibiotics for agricultural needs. Professor Gottlieb works only with those antibiotics which take in /food/ through roots and penetrate into plants.

The laboratory has a good tradition of searching out antibiotics. Professor Gottlieb and his co-workers have discovered endomycin and filippin /Transliterated/. Simultaneously with Ehrlich, Doctor Gottlieb discovered the widely-known and highly-effective chloramphenicol.

B. The second problem of the laboratory is the study of the behavior of antibiotic substances in the soil. A great amount of work has been done by Professor Gottlieb on the adsorption of antibiotics in the soil. The professor's experimental work confirms the investigation of Soviet scientists on the great biological role of antibiotics in the life of the soil.

Doctor Gottlieb is a champion of the view of the great role of antibiotic substances in the interrelationships of microorganisms in nature. Gottlieb showed that antibiotic substances manifest their antimicrobic action in the soil and that neutral and acid antibiotics are not adsorbed in the soil.

C. A large portion of the work of the laboratory is devoted to studying the metabolism of the producers of neomycin and chloramphenicol. Interesting work has been done in the laboratory which shows that steroids are antagonists of polyene antibiotics.

Professor Gottlieb's laboratory has worked for many years in cooperation with the head of the Department of Biochemistry of this university, Doctor Carter.

8. The Laboratory of Doctor Carter in the University of Illinois

Professor Carter is one of the greatest biochemists who work with microorganisms and enjoys enormous authority among the scientists of the United States as a specialist.

Work is being conducted in Professor Carter's laboratory on study of the structure of streptothricin, filippin /Transliterated/, and neomycin. He has done a great deal of work on identifying different antibiotics of the streptothricin group. It was established that there are six antibiotics in the streptothricin group which are chemically markedly different. In addition to these six antibiotics, still others are being studied at present which, in Professor Carter's opinion, also belong to the streptothricin group.

9. The Northern Regional Laboratory of the US Department of Agriculture.

The Northern Regional Laboratory, which is located in the city of Peoria, Illinois, is a large scientific research institute that is working on the most varied problems of agriculture.

Acquaintance with the laboratory of this institute is of great interest for the specialist in microbiology, as this laboratory is conducting large projects on antibiotics, taxonomy, and the study of growth factors.

Scientists who are well known to Soviet specialists are working in the laboratory: Benedict, Stodola, Hesseltine, and Pridgeim /Transliterated/.

Professor Stodola is one of the greatest specialists in the United States in the field of the biochemistry of microorganisms. He is the discoverer of ghiberellin A and ghiberellic acid, which were discovered by him independently and simultaneously with the English scientist Brayns /Transliterated/.

Of recent years the section has been working on problems connected with the extraction and study of ghiberellins. The section is closely linked with many companies that produce ghiberellin--the Pfizer, Eli Lilly, Abbott, and Merck Companies. At present Professor Stodola is completing a monograph on ghiberellins which is expected to be out in 1959.

Doctor Benedict's section, in which Professor Pridgeim also works, is working on a search for antibiotic substances of Actinomyces origin for the needs of plant culture. The greatest emphasis in this work is placed on searching for fungicidal antibiotics.

The taxonomy of Actinomyces constitutes a large portion of the work of Professor Benedict's section.

The taxonomy of Actinomyces in this section is constructed on principles very close to those of Soviet research workers. All classification of the Actinomyces producers of antibiotic substances is based upon morphological criteria. On this basis the section has a large collection of Actinomyces producers of antibiotic substances which can be compared only with the museum producers of antibiotic substances in the Institute of Microbiology of Rutgers University.

The Northern Regional Laboratory has the best collection of yeast organisms in the world which is in charge of Professor Hesseltine.

The laboratory has splendid semiproduction facilities. American scientists state that this is the best semiproduction facility in non-company research institutes.

The Northern Regional Laboratory is coordinating a number of research projects on the use and study of antibiotics for the needs of plant culture. It is linked with a number of agricultural stations which are using antibiotics both for combatting phytopathogenic microorganisms and for accelerating the growth and development of animals.

Large projects are conducted in laboratory facilities to study the conditions of the fermentation of the producers of certain antibiotics. The same facilities are used to accumulate antibiotic substances for the needs of animal husbandry.

It appears to us that the Northern Regional Laboratory is at present the center of the work being done in the taxonomy of Actinomyces.

It is impossible to describe the work of all the microbiological institutions with which we became more or less familiar in a brief article. Many of these institutes have been visited by Soviet specialists and the research work being done in them is sufficiently well known.

It seems necessary to us to discuss the work of the Rockefeller Institute, which is of interest to Soviet specialists.

10. The Rockefeller Institute

As is well known, the Rockefeller Institute is a large scientific research institute of medical studies in which work on morphology and cytology is harmoniously combined with physiology, biochemistry, and biophysics. It seems rational to us to dwell on three departments of this institute.

The laboratory of Doctor Dyubo /Transliterated/ is not very large. It studies three problems: a) determining the conditions for cultivating the tubercelosis bacillus when it is grown in deep cultures; b) isolating the chemically pure substance from the cell of the tuberculosis bacillus which would possess the capability of immunzing the human organism; c) working on phagocytosis. All these studies are being carried on very intensely. The development of the tuberculosis bacillus is being studied in the department in accordance with the composition of amino acids and proteins in the medium.

Professor Dyubo showed that the pH value plays a large role in the mechanism of phagocytosis. In addition, the production of lysocine, which inhibits the development of Gram-positive microflora, is of considerable importance.

It was discovered in the laboratory that, in addition to lysocine, phagocytin, which is secreted by cells, is of great importance in phagocytosis. According to Dyubo's data, phagocytin inhibits the development of Gram-positive microorganisms.

The laboratory of Nobel Prize winner Professor Lyman Craig is occupied with developing the newest methods for separation of albumens. The counter-flow method for separation is widely used in the laboratory. By using the system of solvents developed by Craig, sufficiently good results were obtained in separating the albumens of blood serum. Curves with pronounced peaks were obtained from the albumens of the serum.

A special type of dialysis, counter flow dialysis, has been developed in the laboratory. This very new method is in the stage of development. Very hopeful results were obtained. The laboratory is equipped with several batteries of dialysis cells.

Doctor Craig is continuing his research in the field of study of the structure of polypeptide antibiotics. At present he is working on establishing the structure of two antibiotics of polypeptide origin. The basic method is counter-flow partition. Methods have been developed in the laboratory for using the method of counter flow partition to determine the molecular weight of polypeptides. According to Craig, this principle can be used for other groups of chemical substances, too.

Craig's laboratory is splendidly equipped. As the discoverer of the method of counter flow partition /protivotochnoye raspredeleniye/, Professor Craig is now perfecting this method which is widely used throughout the entire world. The largest apparatus in the world for counter flow partition, consisting of a thousand tubes, has been set up in the laboratory. This apparatus is completely automatized.

The biophysics laboratory of Professor Zworykin has a small staff which includes a number of biologists and physicists. This laboratory is brilliantly equipped. Equipment is obtained from the Rockefeller Institute and from the very large Radio Corporation of America.

Professor Zworykin is one of the discoverers of color television and one of the designers of the electron microscope.

At present, an ultraviolet, color television microscope has been designed in Professor Zworykin's laboratory which will permit examining the living cell without staining. Some organic compounds of the cell can be recognized directly by their color on the screen, for example, nucleic acid. In some cases it will also be possible to determine their number by measuring the absorption of ultraviolet light on an oscillograph. In this microscope it will be possible to take color motion pictures of a living cell, a thing which naturally cannot be accomplished in an ordinary microscope which employs light.

Professor Zworykin is the leader in the United States in the work on the problem of applying electronics to biology and medicine.

A pill instrument was designed in his laboratory which is a very small semiconductor transmitter designed in the form of a pill. After swallowing this pill, the patient is placed near a special receiver instrument. As the pill passes through the digestive tract, this instrument records the temperatures of all sections of the intestine and the pressure in the stomach is also determined by another pill. Professor Zworykin has completed work on manufacturing a pill for measuring pH values in all sections of the intestinal tract.

All these "pills" have been and are being tested successfully in clinical institutions in the United States.

It is necessary to note the great interest that the co-workers of the Rockefeller Institute have in Soviet science. A very large number of the scientific workers of the Rockefeller Institute are studying the Russian language intensively.

The president of the Rockefeller Institute is Doctor Brunk, who is at the same time president of the National Academy of Science.

Education in Microbiology in the United States

We believe it is essential to discuss the problems of education in microbiology in the United States, as it would be desirable to take into account certain special features of this education in the training of specialists in the Soviet Union.

Higher education in biology in the United States has been set considerably lower than in the Soviet Union. After completing high school, which is on a level of learning lower than in the USSR, the biology student in an American university studies only four years there, during which time he takes a number of general educational subjects which are taken in middle /high/ school in our country.

In contrast to this, the general theoretical training of Doctors of Science in the United States, which is equivalent to our candidate's post-graduate work, seems good to us. All microbiologists who are studying for a doctor's degree are obliged to pass a difficult course in inorganic, organic, and biological chemistry.

In some cases (far from rare), they also study physical chemistry.

In order to train Doctors of Science in the field of microbiology, chemists of very high qualifications are brought in to give a very "stiff" test to candidates for the doctoral degree.

Thus, when they receive the degree of Doctor of Science, microbiologists are very well trained in different fields of chemistry.

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